Management of acute kidney injury during critical illness – what is on the horizon?

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Over the past decade, the pace of acute kidney injury (AKI) research and innovation has accelerated. Although much of the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) AKI guideline remains state of the art [1], our understanding of the pathophysiology of AKI has improved and new tools to diagnose and manage AKI have been developed, in particular new biomarkers, improved imaging and monitoring techniques, new decision-support programs and the application of artificial intelligence. Furthermore, many promising drugs and compounds are entering clinical trials. As a result, new opportunities for prevention, early intervention and personalized management are on the horizon.

AKI is a heterogeneous disease with multiple different subphenotypes and variable outcomes [2–4]. Patients who survive AKI face an increased risk of chronic kidney disease, premature long-term dialysis and increased mortality but not everyone with AKI has a poor outcome. To date, most clinical trials examining pharmacotherapy, novel biologics and intensity of renal replacement therapy (RRT) have been negative. One postulated reason for this dearth of positive trials is the delay in diagnosing and monitoring AKI due to a reliance on serum creatinine and urine output [5]. Another contributing factor is our approach of treating AKI as a single entity without differentiating between different causes and subtypes.

The discovery of new kidney biomarkers has not only improved our understanding of the pathophysiology of AKI and allowed an earlier diagnosis of AKI, biomarkers have also identified high-risk patients and AKI subtypes and provided opportunities for biomarker-guided management [6,7]. Current evidence supports the utilization of new biomarkers in routine clinical practice but substantial gaps in knowledge remain [8–11,30]. Determining the cause and sub-type of AKI is also essential for future clinical trials. As an example, Bhatraju *et al.* identified two molecularly distinct subphenotypes of AKI with different clinical outcomes and responses to vasopressin [2]. Not surprisingly, experts have called for a revision of the KDIGO AKI consensus definition and suggested to incorporate cause, pathophysiology and potentially new kidney biomarkers [12].

Creatinine and urine output are traditionally used to monitor renal function and the response to treatment. Real-time assessment and monitoring of renal function are not routinely available in clinical practice at present. However, new technologies and imaging techniques have been developed and are undergoing clinical evaluation [13–17]. This prospect of real-time monitoring of glomerular filtration is exciting with the potential to individualize patient care, identify renal injury early and improve patient outcomes.

There is no doubt that artificial intelligence will be increasingly used in medicine, including in critical care nephrology. By utilising routine electronic health records, advanced information technology systems and artificial intelligence have developed models to detect specific AKI patterns, identify high-risk cohorts and predict outcomes [18,19]. Although only a few have been validated in external cohorts to date, this collaboration between computer science and medicine demonstrates the immense possibilities for risk prediction and clinical management in future. Prospective external validation of newly developed models is necessary, followed by prospective interventional trials.

To date, management of AKI is supportive with focus on haemodynamic and fluid management and avoidance of nephrotoxic drugs [1,20–22]. At present, no specific medication is available to prevent or treat AKI. However, as a result of better understanding of the pathophysiology of AKI, a variety of crucial pathways have been identified that may be targeted, in particular renal haemodynamics, oxidative and mitochondrial stress, cellular metabolism and repair, inflammation and apoptosis [23,24]. Many promising compounds are currently

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undergoing clinical trials with the potential to transform patient care.

It is very likely that the ongoing technical advances and progress in information technology and computer science will impact the practice of RRT, too. There is hope that in future, the provision of RRT will be more individualised with regards to timing, fluid removal and solute control, as directed by the patient's needs (concept of precision medicine) [25].

Finally, there is general consensus that AKI care does not stop at discharge from the hospital [26]. However, there is no agreement who should be followed up and what follow-up care should look like [27,28]. Several prospective trials are currently in progress AKI with the prospect of informing future AKI aftercare.

In conclusion, the past decade has seen many exciting developments in the field of AKI. There is high hope that we will be able to untangle the complex and heterogeneous clinical syndrome of AKI and identify those who are at highest risk and those who are likely to respond to a particular therapy [29]. Thus, we may be one step closer to personalized precision medicine and improved patient-centred outcomes in AKI. This issue of *Current Opinion in Critical Care* includes contributions from experts in the field who provide a detailed overview of technologies and developments on the horizon.

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